

CLAIMS

1) - A compound of formula (I):

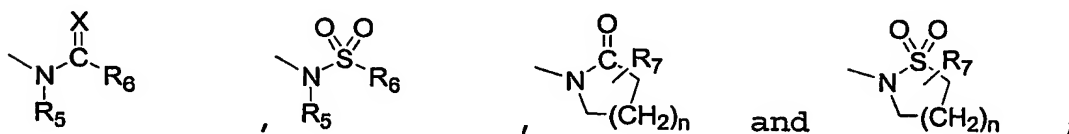


(I)

wherein

R_1 is selected from the group consisting of phenyl, pyridyl, pyrimidinyl, triazinyl, N-oxide-pyridyl, thienyl, furyl, thiazolyl and oxazolyl, each R_1 being optionally substituted with an R_2 group;

R_2 is selected from the group consisting of alkyl(C_1-C_6), cycloalkyl(C_3-C_6), alkenyl(C_2-C_6), alkynyl(C_2-C_6), alkoxy(C_1-C_6), CF_3 , CN, SO_2-R_3 , NO_2 , $NH-R_3$, NR_3R_4 , COR_5 , $CONHR_5$, $COOR_5$,



R_3 and R_4 are independently selected from the group consisting of alkyl(C_1-C_6), cycloalkyl(C_3-C_6), aryl and heteroaryl;

R_5 is selected from the group consisting of hydrogen, alkyl(C_1-C_6), alkenyl(C_2-C_6), alkynyl(C_2-C_6) and cycloalkyl(C_3-C_6);

R_6 is selected from the group consisting of alkyl(C_1-C_6), cycloalkyl(C_3-C_6), alkoxy(C_1-C_6), NH -alkyl(C_1-C_6), N (dialkyl(C_1-C_6)), alkyl(C_1-C_6)-O-alkyl(C_1-C_6), alkyl(C_1-C_6)- NH -alkyl(C_1-C_6), alkyl(C_1-C_6)- N (dialkyl(C_1-C_6)),

phenyl, monosubstituted phenyl, furyl, thienyl, thiazolyl and pyridyl;

R_7 is selected from the group consisting of hydrogen, alkyl(C_1-C_6), cycloalkyl(C_3-C_6), aryl and substituted or unsubstituted heteroaryl;

R_8 is selected from the group consisting of hydrogen, alkyl(C_1-C_6), CF_3 , CN, $CO-R_9$ and SO_2-R_9 ;

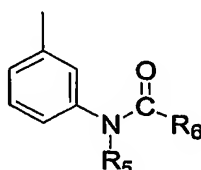
R_9 is selected from the group consisting of hydrogen, alkyl(C_1-C_6), phenyl, substituted phenyl and substituted or unsubstituted heteroaryl;

X is O, S or NR_8 ; and

n is an integer 1, 2 or 3;

and their pharmaceutically acceptable salts.

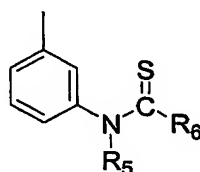
2) - A compound according to claim 1, wherein R_1 is



and wherein R_5 and R_6 are as described for formula (I).

3) - A compound according to claim 2, wherein R_5 is selected from the group consisting of methyl, ethyl, n-propyl, i-propyl, n-butyl, cyclopropyl and 2-propynyl; and R_6 is selected from the group consisting of methyl, ethyl, n-propyl, n-butyl, phenyl and 4-methoxy-phenyl.

4) - A compound according to claim 1, wherein R_1 is



and wherein R_5 and R_6 are as described for formula (I).

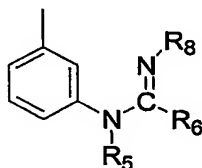
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5) - A compound according to claim 4, wherein R_5 is selected from the group consisting of methyl, ethyl, n-propyl, i-propyl, n-butyl, cyclopropyl and 2-propynyl; and R_6 is selected from the group consisting of methyl, ethyl, n-propyl, n-butyl, phenyl and 4-methoxy-phenyl

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6) - A compound according to claim 1, wherein R_1 is

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and wherein R_5 , R_6 and R_8 are as defined for formula (I).

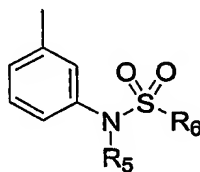
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7) - A compound according to claim 6, wherein R_5 is selected from the group consisting of methyl, ethyl, n-propyl, i-propyl, n-butyl, cyclopropyl and 2-propynyl; R_6 is selected from the group consisting of methyl, ethyl, n-propyl, n-butyl, phenyl and 4-methoxy-phenyl; and R_8 is selected from the group consisting of hydrogen, methyl and CN.

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8) - A compound according to claim 1, wherein R_1 is

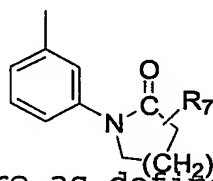
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and wherein R_5 and R_6 are as defined for formula (I).

9) - A compound according to claim 8, wherein R_5 is selected from the group consisting of methyl, ethyl, n-propyl, i-propyl, n-butyl, cyclopropyl and 2-propynyl; and R_6 is selected from the group consisting of methyl, ethyl, n-propyl, i-propyl, n-butyl, phenyl and 4-methoxy-phenyl.

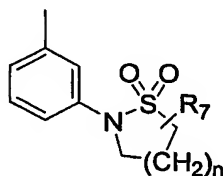
10) - A compound according to claim 1, wherein R_1 is



and wherein n and R_7 are as defined for formula (I).

11) - A compound according to claim 10, wherein n is 1 and R_7 is hydrogen.

12) - A compound according to claim 1, wherein R_1 is



and wherein n and R_7 are as defined for formula (I).

13) - A compound according to claim 12, wherein n is 1 and R_7 is hydrogen.

14) - A compound according to claim 1, wherein R_1 is selected from the group consisting of phenyl, 2-trifluoromethylphenyl, 3-trifluoromethylphenyl, 4-

trifluoromethylphenyl, furan-2-yl, thiophen-2-yl, pyridin-2-yl, pyridin-3-yl and pyridin-4-yl.

15) - A compound according to claims 2 and 3, wherein said compound is selected from the group consisting of:

N-ethyl-N-[3-(3-nitro-pyrazolo[1,5-a]pyrimidin-7-yl)-phenyl]-acetamide;

N-methyl-N-[3-(3-nitro-pyrazolo[1,5-a]pyrimidin-7-yl)-phenyl]-acetamide;

N-[3-(3-nitro-pyrazolo[1,5-a]pyrimidin-7-yl)-phenyl]-N-(n-propyl)-acetamide;

N-(n-butyl)-N-[3-(3-nitro-pyrazolo[1,5-a]pyrimidin-7-yl)-phenyl]-acetamide; and

N-[3-(3-nitro-pyrazolo[1,5-a]pyrimidin-7-yl)-phenyl]-N-(2-propynyl)-acetamide.

16) - A compound according to claims 8 and 9, wherein said compound is selected from the group consisting of:

N-ethyl-N-[3-(3-nitro-pyrazolo[1,5-a]pyrimidin-7-yl)-phenyl]-methanesulfonamide;

N-ethyl-N-[3-(3-nitro-pyrazolo[1,5-a]pyrimidin-7-yl)-phenyl]-4-methoxy-benzenesulfonamide;

N-ethyl-N-[3-(3-nitro-pyrazolo[1,5-a]pyrimidin-7-yl)-phenyl]-benzenesulfonamide;

N-methyl-N-[3-(3-nitro-pyrazolo[1,5-a]pyrimidin-7-yl)-phenyl]-methanesulfonamide;

N-(n-butyl)-N-[3-(3-nitro-pyrazolo[1,5-a]pyrimidin-7-yl)-phenyl]-4-methoxy-benzenesulfonamide;

N-[3-(3-nitro-pyrazolo[1,5-a]pyrimidin-7-yl)-phenyl]-N-(n-propyl)-4-methoxy-benzenesulfonamide;

N-methyl-N- [3- (3-nitro-pyrazolo [1,5-a]pyrimidin-7-yl) -phenyl] -4-methoxy-benzenesulfonamide;

N- (n-butyl) -N- [3- (3-nitro-pyrazolo [1,5-a]pyrimidin-7-yl) -phenyl] -4-benzenesulfonamide;

5 N- [3- (3-nitro-pyrazolo [1,5-a]pyrimidin-7-yl) -phenyl] -N- (n-propyl) -benzenesulfonamide;

N-methyl-N- [3- (3-nitro-pyrazolo [1,5-a]pyrimidin-7-yl) -phenyl] -4-benzenesulfonamide;

10 N- [3- (3-nitro-pyrazolo [1,5-a]pyrimidin-7-yl) -phenyl] -N- (n-propyl) -methanesulfonamide;

N- (n-butyl) -N- [3- (3-nitro-pyrazolo [1,5-a]pyrimidin-7-yl) -phenyl] -methanesulfonamide;

N- [3- (3-nitro-pyrazolo [1,5-a]pyrimidin-7-yl) -phenyl] -N- (prop-2-ynyl) -methanesulfonamide;

15 N- [3- (3-nitro-pyrazolo [1,5-a]pyrimidin-7-yl) -phenyl] -N- (n-propyl) -ethanesulfonamide;

N- [3- (3-nitro-pyrazolo [1,5-a]pyrimidin-7-yl) -phenyl] -N- (n-ethyl) -ethanesulfonamide;

20 N- [3- (3-nitro-pyrazolo [1,5-a]pyrimidin-7-yl) -phenyl] -N- (n-prop-2-ynyl) -propane-2-sulfonamide;

N- [3- (3-nitro-pyrazolo [1,5-a]pyrimidin-7-yl) -phenyl] -N-methyl-ethanesulfonamide;

N- [3- (3-nitro-pyrazolo [1,5-a]pyrimidin-7-yl) -phenyl] -N- (n-butyl) -ethanesulfonamide;

25 N- [3- (3-nitro-pyrazolo [1,5-a]pyrimidin-7-yl) -phenyl] -N-methyl-propane-2-sulfonamide;

N- [3- (3-nitro-pyrazolo [1,5-a]pyrimidin-7-yl) -phenyl] -N-ethyl-propane-2-sulfonamide;

30 N- [3- (3-nitro-pyrazolo [1,5-a]pyrimidin-7-yl) -phenyl] -N- (n-butyl) -propane-2-sulfonamide; and

N- [3- (3-nitro-pyrazolo [1,5-a]pyrimidin-7-yl) -phenyl] -N- (n-propyl) -propane-2-sulfonamide.

17) - A compound according to claims 10 and 11, wherein said compound is 1-[3-(3-nitro-pyrazolo[1,5-a]pyrimidin-7-yl)-phenyl]-pyrrolidin-2-one.

5 18) - A compound according to claims 12 and 13, wherein said compound is 7-(3-(2-isothiazolydiny1-1,1-dioxide)-phenyl)-3-nitro-pyrazolo[1,5-a]pyrimidine.

10 19) - A compound according to claim 14, wherein said compound is selected from the group consisting of:

3-nitro-7-phenyl-pyrazolo[1,5-a]pyrimidine;
3-nitro-7-(2-trifluoromethyl-phenyl)-pyrazolo[1,5-a]pyrimidine;

15 3-nitro-7-(3-trifluoromethyl-phenyl)-pyrazolo[1,5-a]pyrimidine;

3-nitro-7-(4-trifluoromethyl-phenyl)-pyrazolo[1,5-a]pyrimidine;

7-furan-2-yl-3-nitro-pyrazolo[1,5-a]pyrimidine;

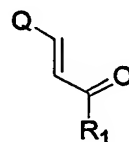
3-nitro-7-thiophen-2-yl-pyrazolo[1,5-a]pyrimidine;

20 3-nitro-7-pyridin-2-yl-pyrazolo[1,5-a]pyrimidine;

3-nitro-7-pyridin-3-yl-pyrazolo[1,5-a]pyrimidine; and

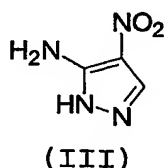
3-nitro-7-pyridin-4-yl-pyrazolo[1,5-a]pyrimidine;

25 20) - A process for preparing a compound of formula (I) or a pharmaceutically acceptable salt thereof, according to claim 1, comprising reacting intermediate (II):



(II)

wherein R_1 is as defined for (I) and Q is an appropriate leaving group selected from the group consisting of N(dialkyl(C_1-C_6)), alkylthio(C_1-C_6) and alkoxy(C_1-C_6), with 4-nitro-2H-pyrazol-3-ylamine (III):



10 and alternatively, treatment of the compounds of claim 1, in the form of free base, with an acid to form a salt thereof.

21) - A process according to claim 20, comprising utilizing the intermediate of formula (II) where Q is selected from the group consisting of dimethylamino, methylthio and methoxy.

22) - A method for treating or preventing diseases associated with $GABA_A$ receptor modulation in a mammal which comprises administering to said mammal an effective amount of a compound of claim 1.

23) A method for treating or preventing diseases associated with α_1 - $GABA_A$ receptor modulation in a mammal which comprises administering to said mammal an effective amount of a compound of claim 1.

24) - A method for treating or preventing diseases associated with α_2 - $GABA_A$ receptor modulation in a mammal which comprises administering to said mammal an effective amount of a compound of claim 1.

25) - A method for treating or preventing anxiety in a mammal which comprises administering to said mammal an effective amount of a compound of claim 1.

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26) - A method for treating or preventing epilepsy in a mammal which comprises administering to said mammal an effective amount of a compound of claim 1.

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27) - A method for treating or preventing sleep disorders in a mammal which comprises administering to said mammal an effective amount of a compound of claim 1.

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28) - A method for treating or preventing insomnia in a mammal which comprises administering to said mammal an effective amount of a compound of claim 1.

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29) - A method for inducing sedation-hypnosis in a mammal which comprises administering to said mammal an effective amount of a compound of claim 1.

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30) - A method for inducing anesthesia in a mammal which comprises administering to said mammal an effective amount of a compound of claim 1.

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31) - A method for modulating the necessary time to induce sleep and its duration in a mammal which comprises administering to said mammal an effective amount of a compound of claim 1.

32) - A method for inducing muscle relaxation in a mammal which comprises administering to said mammal an effective amount of a compound of claim 1.

5 33) - A composition comprising a compound of claim 1 in association with a therapeutically inert carrier.

34) - The use of a compound of claim 1 for preparing a medicament for treating or preventing diseases associated with GABA_A receptor modulation.

10 35) - The use of claim 33 wherein the diseases are associated with α_1 -GABA_A or α_2 -GABA_A receptor modulation.

15 36) - The use of a compound of claim 1 for preparing a medicament for treating or preventing anxiety, epilepsy, sleep disorders, insomnia, for inducing sedation-hypnosis, anesthesia or muscle relaxation or for modulating the necessary time to include sleep and its duration.

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